CHROMIUM/BIOTIN TREATMENT OF TYPE II DIABETES

RELATED APPLICATIONS

This is a continuation-in-part of allowed U.S. application Ser. No. 08/908,819,filed Aug. 8, 1997, now U.S. Pat. No. 5,789,401 the entire contents of which are hereby incorporated by reference.

FIELD OF THE INVENTION

The present invention relates to the treatment of adult-onset non-insulin dependent (Type II) diabetes. More specifically, the invention relates to the treatment of Type II diabetes by administering chromic picolinate and biotin.

BACKGROUND OF THE INVENTION

Diabetes mellitus is known to affect at least 10 million Americans, and millions more may unknowingly have the disease. In the form of this disease known as Type II, non-insulin dependent or adult-onset (as opposed to juvenile diabetes or Type I), the pancreas often continues to secrete normal amounts of insulin. However, this insulin is ineffective in preventing the symptoms of diabetes which include hyperglycemia, impaired carbohydrate metabolism, glycosuria and decreased insulin sensitivity. These symptoms, if left untreated, often lead to severe complications.

Current drugs used for managing Type II diabetes fall within two classes of compounds: the biguanides and the sulfonylureas. The biguanides, e.g. metformin, are believed to prevent excessive hepatic gluconeogenesis. The sulfonylureas, e.g. tolbutamide and glyburide, lower plasma glucose primarily by stimulating insulin secretion, by enhancing insulin effects in some target tissues and by inhibiting hepatic glucose synthesis.

U.S. Pat. No. 4,315,927 discloses that when selected essential metals are administered to mammals as exogenously synthesized coordination complexes of picolinic acid, they are directly available for absorption without competition from other metals. These complexes are safe, inexpensive, biocompatible and easy to produce.

U.S. Pat. No. 5,087,623 describes the administration of chromic tripicolinate for the treatment of Type II diabetes in doses which provide between 50 and 500 μg of chromium. The U.S. Recommended Daily Allowance for chromium is 50–200 μg. Although a small decrease in glycosylated hemoglobin, an accurate indicator of blood glucose levels, was observed, the 10.4% value obtained after chromic tripicolinate treatment was still will within the diabetic range.

International Patent Application No. PCT/US96/06493 discloses the administration of high ("supranutritional") doses of chromium (1,000 to 10,000 μg/day) to individuals with Type II diabetes. Individuals who received 1,000 μg chromium per day as chromic tripicolinate exhibited a 30% decrease in glycosylated hemoglobin and a similar reduction in fasting and postprandial glucose levels.

Biotin is the prosthetic group for a number of carboxylation reactions, the most notable being pyruvate carboxylase which is involved in gluconeogenesis and replenishment of the citric acid cycle, and acetyl CoA carboxylase which plays a role in fatty acid biosynthesis. The safe and adequate recommended daily intake of biotin is 100–300 μg, although no side effects or toxicities were noted in previous clinical studies with oral biotin intakes of up to 200 mg daily (Mock et al, in *Present Knowledge in Nutrition,* seventh edition, Ziegler, E. et al., eds., ILSI Press, Washington, D.C., 1996, pp. 220–235). Supranutritional doses of biotin have been shown to have therapeutic utility in diabetes. High-dose oral or parenteral biotin has been shown to improve oral glucose tolerance in diabetic KK mice (Reddi et al., *Life Sci.,* 42:1323–1330, 1988), rats made diabetic by injection with streptozotocin (Zhang et al., 16th International Congress of Nutrition, Montreal, 1997, abstract book, p. 264) and in pre-diabetic Otsuka Long-Evans Tokushima Fatty rats (Zhang et al., *J Nutr. Sci. Vitaminol.* 42:517–526, 1996).

In a clinical study, Coggeshall et al. (*Ann. N.Y. Acad. Sci,* 447:387–392, 1985) demonstrated that a daily oral dose of biotin of 16 mg lowered fasting plasma glucose levels in Type I diabetics in whom insulin injections had been temporarily discontinued. Maebashi et al. (*J Clin. Biochem. Nutr.* 14:211–218, 1993) showed that administration of 3 mg biotin three times per day to poorly-controlled type II diabetics resulted in improved pancreatic beta cell function as evidenced by the fact that fasting insulin levels did not decline in biotin-treated subjects despite the sharp decline in glucose levels.

There is a constant need for effective treatments for type II diabetes. The present invention addresses this need by providing a safe, inexpensive, drug-free therapeutic agent.

SUMMARY OF THE INVENTION

One embodiment of the present invention is a method for reducing hyperglycemia and stabilizing the level of serum glucose comprising administering to an individual in need thereof between about 50 and 1,000 micrograms per day of chromium as synthetic chromic tripicolinate in combination with between about 25 μg and 200 mg per day of biotin, the amounts of chromic tripicolinate and biotin being selected together to provide a greater than additive effect. Preferably, the amount of chromium administered as synthetic chromic tripicolinate is between 500 and 1,000 micrograms per day. Advantageously, the amount of biotin administered per day is between about 1 mg and 100 mg. In one aspect of this preferred embodiment, the chromic tripicolinate is in a pharmaceutically acceptable carrier. In another aspect of this preferred embodiment, the biotin is in a pharmaceutically acceptable carrier. Preferably, the biotin is orally administered. Advantageously, the chromic tripicolinate is orally administered. Preferably, the chromic tripicolinate is parenterally administered. In another aspect of this preferred embodiment, the biotin is parenterally administered.

The present invention also provides a pharmaceutical composition comprising chromium as synthetic chromic tripicolinate and biotin, wherein the ratio of chromium to biotin is between about 2:1 and 1:200 (w/w), the amounts of chromic tripicolinate and biotin being selected together to provide a greater than additive effect.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention includes the discovery that doses of chromium from the highest RDA amount up to five times this amount, administered in the form of chromic picolinate, combined with either low or high doses of biotin, promote significant reduction in blood glucose levels and stabilize blood glucose levels in individuals with type II diabetes. This reduction is markedly greater than what would be expected when either component is administered alone, thus indicating a synergistic effect.

The synthesis of chromic picolinates is described in U.S. Pat. No. 5,087,623, the entire contents of which are hereby